REMARKS/ARGUMENTS

Applicant respectfully requests reconsideration and allowance of this application in view of the amendments above and the following comments. Applicant respectfully submits that the amendments are fairly based on the specification and respectfully requests their entry.

35 U.S.C. § 112, SECOND PARAGRAPH REJECTION OF CLAIMS 1, 3, 5-9 & 12-18

Claims 1, 3, 5-9 & 12-18 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Specifically, the Examiner objects to what is viewed as vague and confusing language and a lack of antecedent basis for terms appearing in dependent claims. Applicant respectfully traverses this rejection for the reasons set forth below.

Regarding the above rejection as applied to claim 1, step d), with respect to the phrase "such that a portion of said signal moiety is caused to be bound to said first component" and its perceived meaning, Applicant points out that the phrase has been amended above. Applicant has amended claim 1, step d) to recite "such that a portion of the amount of said second component carrying said signal moiety is caused to be bound to said first component". Applicant submits that the amended language above, is responsive to the Examiner's question (which appears at lines 2-4, on page 3 of the

Office Action mailed November 12, 2003) concerning the language and that the amended language clarifies the meaning of step d) and is now definite.

Regarding the above rejection as applied to claim 1, step f), parts i) and ii) and the perceived lack of clarity regarding how the signal and the detectable label are measured and determined differentially, Applicant respectfully submits that The specification provides ample guidance to one of ordinary skill in the art to recognize the various structural and functional relationships between the assay components. The person skilled and knowledgeable in the field of flow cytometry and the fluorescence assay processes using this technique would readily appreciate that, where the signal moiety and the detectable label of the invention comprise spectrally distinguishable fluors, they may be readily independently measured by flow cytometry.

Claim 1 uses two different types of terminology for: 1) the bead/sample identifiers, which is/are detectable label(s) and 2) the assay identifier/indicator on said "second component", which carries a signal moiety. Where fluorescent labels are used for both, the specification makes it clear that the fluorescent labels used for tagging ligands or substrates (i.e., second component) must be "spectrally distinct and distinguishable from any fluorescent dye used for bead identification." (page 9, line 3).

Therefore, there should be no confusion between the detectable label indicating the sample identity and the signal moiety, which provides signal measurements from which values for the test compound (e.g., concentration, biological activity) can be deduced.

Given the various possible binding, chemical or enzymatic reactions that may take place, as set forth in the specification, it would be apparent to one of ordinary skill in the art, how the signal moiety can provide the desired indications. Therefore, Applicant submits that step f), parts i) and ii) are definite when read in view of the specification.

Regarding the above rejection and the Examiner's concerns regarding cross-reactivity upon combining samples (p. 3, paragraph 2 of the Office Action), Applicant respectfully submits that cross-reactivity is not of concern with the claimed method. Applicant submits that if a series of assays (e.g. receptor binding assays) is carried out separately and in parallel such that binding in each reaction comes to an equilibrium state between a first component (receptor), a second component (labeled ligand) and any receptor active component in each sample, then the rapid mixing and analysis by flow cytometry will retain the association between the first and second components present in the reactions prior to mixing. Furthermore, the presence of unbound components will not interfere with analysis by flow cytometry because fluorescence not associated with beads is not measured due to the optical configuration which is the basis of the analysis technique.

Regarding the above rejection and the Examiner's concerns regarding the presence of the single compound to be tested in the binding assay (p. 3, paragraph 2 of the Office Action), Applicant respectfully points out that claim 1 has been amended above at step "c)" to insert the phrase --having a single compound to be tested-- following the term "N samples". Thus, the presence of the "single compound" in each sample, in the assay is now clear and basis for the Examiner's concern has now been eliminated.

Regarding the above rejection and the Examiner's concerns regarding the measurement of biological activity (p. 3, paragraph 2 of the Office Action), Applicant respectfully points out that measurement of biological activity does not always require intracellular function measurement. Many assays using isolated or recombinant proteins can be used to determine biological activity without measurement of activity in intact cells. In all assays, the nature of the information obtained will be determined by the components used. For example, if it is desired only to detect the presence or absence of a compound or its concentration, then an antibody-binding assay will yield such information. If alternatively, it is wished to measure biological activity, then substitution, for example, of a recombinant receptor protein in the same assay will yield the desired result. Therefore, Applicant respectfully submits that there is no concern regarding measurement of biological activity

Regarding the above rejection as applied to claim 6, with respect to the term "reagent" as it appears in line 1 and as lacking antecedent basis, Applicant respectfully points out that claim 6 has been amended above to delete "or reagent" from line 1 of claim 6. Thus, the basis for the above rejection as applied to claim 6 has been eliminated.

Regarding the above rejection as applied to claim 12, step f), parts i) and ii) and the Examiner's concerns regarding perceived lack of clarity in how the signal and the detectable label are measured and determined differentially, cross-reactivity and measuring biological activity, Applicant respectfully submits that these concerns have been addressed above under Applicant's response to corresponding concerns in claim 1. Therefore, Applicant respectfully submits that claim 12, step f), parts i) and ii) are definite when read in view of the specification.

Regarding the above rejection as applied to claim 15, with respect to the term "reactant" as it appears in line 1 and as lacking antecedent basis, Applicant respectfully points out that claim 15 has been amended above to delete "reactant or" from line 1 of claim 15. Thus, the basis for the above rejection as applied to claim 15 has been eliminated. In view of the amendments and comments above, Applicant respectfully requests that the above rejections under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

35 U.S.C. § 103(a) REJECTION OF CLAIMS 1, 3, 5-7, 9, 12-16 and 18

Claims 1, 3, 5-7, 9, 12-16 and 18 are rejected under 35, U.S.C. § 103(a) as being unpatentable over Chandler et al., US 5,981,180 (hereinafter "Chandler") in view of Yamashita et al., US 6,210,900 (hereinafter "Yamashita"). Specifically, in presenting the *prima facie* case of obviousness, the Examiner sets forth elements of the instant invention as claimed, conceding that Chandler fails to disclose the elements. The Examiner continues by presenting the disclosure of Yamashita, which in Applicant's view, fails to supply teaching or motivation to combine the references and arrive at the claimed invention. The Examiner, however, then concludes that it would have been obvious to one of ordinary skill in the art at the time of the instant invention to combined the reaction samples of Chandler into a mixture and apply the analysis methods of Yamashita. Applicant respectfully traverses this rejection for the reasons set forth below.

As previously submitted by Applicant, Chandler in combination with the Yamashita reference does not teach Applicant's inventive method as claimed. Chandler lacks many of the features of Applicant's invention, as set forth by the Examiner at the top of page 6 of the Office Action. Yamashita does not teach the use of a method with pre-existing compounds that are not coupled to beads. Additionally, neither Chandler or Yamashita teaches the addition of multiple samples containing a single compound to be

tested, as instantly claimed. These limitations are present in all of Applicant's claims, either directly or by virtue of their dependence from claim 1 or 12.

The Examiner's "**Response to Arguments**" section of the Office Action dated November 12, 2003, pages 8-9, paragraphs "A" and "B", makes clear why Applicant's previous arguments have not been persuasive. The Examiner's main concern appears to be that the recitation "said samples each containing a single compound to be tested" in claims 1 and 12, has not been given patentable weight because, it occurs in the preamble. In response to the Examiner's concern, Applicant has now amended claims 1 and 12 to insert the phrase - - having a single compound to be tested, - - into step "c)" of claims 1 and 12. Therefore, claims 1 and 12 now read, in pertinent part, "dispensing one of said N samples having a single compound to be tested, into a separate, corresponding one of said N different reaction vessels,".

Applicant respectfully submits that the above amendment to claims 1 and 12 make clear that the "single compound to be tested" in each sample is an element now contained in the body of the claims. Applicant further points out that the application of the compound to be tested is very clearly described in the specification. For example, page 7, line 26 to page 8, line 11 describes equilibrium binding assays in which the reactant may be an immunochemical reagent or a receptor. The compounds to be screened are for example, tested for their effect on the binding, (either antagonistic or

agonistic) to the second member of the binding pair. In such instances, it is therefore clear that the test compound competes with the labeled ligand for binding to its binding partner.

The limitation "single compound to be tested" now in step "c)" of claims 1 and 12, is present in all of Applicant's claims, either directly or by virtue of their dependence form claim 1 or 12. In view of the amendments and comments above and the deficiencies of the cited references, Applicant respectfully submits that the presently claimed invention is patentably nonobvious over the prior art. Thus, it is respectfully requested that the above rejection be reconsidered and withdrawn.

35 U.S.C. § 103(a) REJECTION OF CLAIMS 8 and 17

Claims 8 and 17 are rejected under 35, U.S.C. § 103(a) as being unpatentable over Chandler et al., in view of Yamashita et al., and further in view of Mandecki, US 5,641,634 (hereinafter "Mandecki"). Specifically, the Examiner concedes that Chandler and Yamashita fail to disclose bead populations that are electronically labeled. The Examiner continues by presenting Mandecki, as teaching electronically encoded carrier beads. The Examiner then asserts that it would have been obvious to one of ordinary skill in the art at the time of the instant invention to electronically encode populations of beads as disclosed by Mandecki, in the method of Chandler as modified by Yamashita

because, Mandecki discloses its applicability in muliplex assays. Concluding, the Examiner states that one of ordinary skill in the art would have been motivated to incorporate the teachings of Mandecki into the method of Chandler as modified by Yamashita and because, Mandecki disclosed the advantage thereof, in further detecting and differentiating increased numbers of analytes simultaneously in assays. Applicant respectfully traverses this rejection for the reasons set forth below.

As discussed above, in connection with the rejection of claims 1, 3, 5-7, 9, 12-16 and 18 under 35 U.S.C. § 103(a), the Chandler and Yamashita references do not teach Applicant's inventive method as claimed. Chandler, fails to teach many of the elements of the claimed method. Yamashita does not teach the use of a method with pre-existing compounds that are not coupled to beads. Additionally, neither Chandler or Yamashita teaches the addition of multiple samples containing a single compound to be tested as instantly claimed. These limitations are present in all of Applicant's claims, either directly or by virtue of their dependence from claim 1 or 12.

The above deficiencies of the Chandler and Yamashita references are not remedied by Mandecki. Mandecki does not provide any teachings regarding the addition of multiple samples containing a single compound to be tested. Consequently, the Examiner has not established a *prima facie* case of obviousness, with respect to the inventive method as claimed. In view of the above deficiencies of the cited references

alone or in combination, the presently claimed invention is patentably nonobvious over the prior art. Thus, it is respectfully requested that the above rejection be withdrawn.

Applicant believes that the foregoing constitutes a full and complete response to all outstanding objections and rejections. Applicant further believes that this application is now in condition for immediate allowance. However, should any issues of a minor nature remain, the Examiner is respectfully requested to telephone the undersigned at telephone number (732) 457-8071 so that the issues might be promptly resolved.

Early and favorable action is earnestly solicited.

Respectfully submitted,

AMERSHAM BIOSCIENCES CORP

By: _____
Stephen G. Ryan
Reg. No.: 39,015

Amersham Biosciences Corp
800 Centennial Avenue
P. O. Box 1327
Piscataway, New Jersey 08855-1327

Tel: (732) 457-8071
Fax: (732) 457-8463

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on April 8, 2004.

Signature: _____

Name: Melissa Leck